



Patent  
38-77(15868)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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In re Application of:

JEFFREY M. STAUB, PETER T. J. HAJDUKIEWICZ,  
AND LARRY GILBERTSON

Serial No.: 09/688,851

Filed: October 16, 2000

For: **METHODS AND VECTORS FOR SITE-SPECIFIC  
RECOMBINATION IN PLANT CELL PLASTIDS**

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Group Art Unit: 1638

Examiner: G. Helmer

Atty Docket: 38-77(15868)

REMARKS IN RESPONSE TO  
OFFICE ACTION DATED MARCH 12, 2003

Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

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37 C.F.R. 1.8

I hereby certify that this correspondence is being deposited  
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addressed to: Assistant Commissioner for Patents,  
Alexandria, VA 22313-1450, on the date below:

September 12, 2003

*Michelle Ludwig*  
Michelle Ludwig

Sir:

In response to the Office Action dated March 12, 2003, having a shortened statutory period for response expiring June 12, 2003, applicants submit the following amendments and remarks. This response is being filed with a three month extension of time to render it timely filed. Please amend the application as indicated in the following sections.

**Claim Status and Amendments**

Please consider the claims according to its status as set forth below:

Claims 1-23 (withdrawn)

Claim 24. (currently amended)      A method for performing ~~a plurality of separate~~  
multiple rounds of plastid transformations in a plant cell plastid using the same selectable marker  
gene for selection of transplastomic plants comprising:

introducing into a plant cell a first recombinant DNA sequence comprising a  
construct capable of being integrated into the plastid genome of the plant cell, said  
construct comprising a DNA sequence encoding a selectable marker gene flanked by a  
pair of compatible recombining sites arranged in parallel orientation as direct repeats, to  
produce a plant cell having a plastid containing said first recombinant DNA sequence;

providing a recombinase compatible to said pair of compatible recombining sites  
to said plant cell to permit excision of said selectable marker gene and producing excision  
of said selectable marker gene,

regenerating a transplastomic plant containing said first recombinant DNA  
sequence without said selectable marker gene from said plant cell, ~~and~~

introducing a second recombinant DNA sequence comprising a construct capable  
of being integrated into the plastid genome of the plant cell, said construct comprising a  
second DNA sequence encoding said selectable marker gene into a plant cell of said  
transplastomic plant obtained from said regenerated plant thereby producing a plastid  
having said second recombinant DNA sequence in said plant cell of said transplastomic  
plant; and

producing a transplastomic plant having said first and second recombinant DNA  
sequences introduced sequentially into said plastid using the same selectable marker gene  
for the second recombinant DNA sequence as used for the selection of the first  
recombinant DNA sequence.

25. (previously amended) The method according to Claim 24, wherein said recombinase is provided to said plant cells by introducing a third recombinant DNA sequence comprising in an operably coupled 5' to 3' manner:

a transcriptional initiation region, a plastid targeting region, and a nucleic acid sequence encoding recombinase.

26. (currently amended) The method according to Claim 24, wherein said construct in said first recombinant DNA sequence further comprises a DNA sequence encoding a ~~gene~~DNA sequence of interest other than a selectable marker gene outside of said pair of compatible recombining sites.

Claims 27-31 (canceled).

32. (previously amended) The method according to Claim 24, wherein said pair of compatible recombining sites is selected from the group consisting of Lox, FRT, and R.

Claims 33-35 (withdrawn)

**Preliminary Remarks**

Claims 24-26, 28 and 32 were pending in this application. Claim 28 has been canceled by this amendment. Should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to this document, the Assistant Commissioner is authorized to deduct the fees from the Monsanto Company Deposit Account No. 13-4125. Applicants respectfully request reconsideration of the claims as amended and in view of the following remarks.

**35 U.S.C. § 112, second paragraph rejection**

Applicants have added clarifying language in claim 24 to “complete” the claim and to address the “omitted essential steps” as suggested by the Examiner. Support for these amendments is implicit in the claims as originally filed and in the specification such as on page 16, lines 14-26. The Examiner has also requested correction or clarification of the use of the term “gene” in Claim 24 and subsequent claims. The word “gene” as used in claim 24 refers in each instance to a “selectable marker gene” as that term is used in the specification (such as the phrase “marker gene”) on page 13, lines 24-32 and page 14, lines 1-14. As used therein, gene refers to the structural coding sequence capable of producing a marker gene product for selection of transformed plastids with any necessary regulatory elements to provide for such expression. Thus the phrase “selectable marker gene” is definite and supported by the definitions in the specification. The use of the word “gene” in claim 26 has been amended to recite a “DNA sequence of interest.”

**35 U.S.C. § 112, first paragraph rejection**

Applicants respectfully traverse the rejections based on 35 U.S.C. § 112, first paragraph and request reconsideration in view of the amended claims and the following remarks. It has been asserted by the Examiner that “a plurality of separate transformations” is new matter not supported by the specification as originally filed. It is respectfully submitted that although not supported *in haec verba*, the phrase and concept are implicitly described in the specification. Nevertheless, Applicants have amended the language to recite “multiple rounds of plastid transformations” in claim 24. Support for this phrase is found on page 3, lines 7-9 of the specification as filed. Withdrawal of this ground of rejection is requested.

Regarding the rejection as it pertains to the recombining sites, Applicants have amended the claims to indicate that the recombination sites and the recombinase must be from a compatible recombination system in parallel orientation as direct repeats. Support for this amendment is found on page 8, lines 16-31 of the specification and the description of recombinase systems therein. In view of the foregoing amendments and remarks, it is respectfully submitted that the 35 USC 112, first paragraph rejection must be withdrawn.

### **35 U.S.C. § 103 rejection**

The claims stand rejected under 35 USC 103(a) as being unpatentable over Dale et al and Svab et al. As acknowledged by the Examiner, Dale et al does not teach, disclose or suggest a method of multiple rounds of transforming a plastid using the same selectable marker gene in a manner allowing for the excision of the selectable marker gene. It is also acknowledged by the Examiner that Svab merely teaches plastid transformation, but provides no teaching, disclosure or suggestion to combine such method with a method of multiple transformations using recombination genes allowing for the use of the same selectable marker gene for each round of transformation. The references cited by the Examiner merely provide separate and distinct methodologies with no motivation or suggestion to be found to combine them, much less with any reasonable expectation of success. Thus, the §103 rejection cannot stand. The criterion for a determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that the claimed invention should be carried out and would have a reasonable likelihood of success, viewed in light of the prior art. In re Dow Chemical, 5 USPQ 2d 1529, 1531 (Fed. Cir. 1988); Burlington Industries v Quigg, 3 USPQ 2d 1436, 1438 (Fed. Cir. 1987); In re Hedges, 228 USPQ 685, 687 (Fed. Cir. 1987); Orthopedic Equipment Company v United States, 217 USPQ 193, 200 (Fed. Cir. 1983); and In re Rinehart, 189 USPQ 143, 148 (CCPA 1976). Both the suggestion and the expectation of success must be founded in the prior art, not in the applicants' disclosure. Dow Chemical, 5 USPQ 2d at 1531. It is respectfully submitted that neither the suggestion to perform the claimed method nor any expectation of success is founded in the art cited by the Examiner. Moreover, in order for a combination of references to render an invention obvious, it must be obvious that their teachings can be combined. In re Avery, 186 USPQ 161 (CCPA 1975).

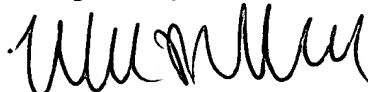
In other words, obviousness cannot be established by combining the teachings of the prior art to produce a claimed invention, absent some teaching, suggestion or incentive supporting the combination. In re Geiger, 2 USPQ 2d 1276 (Fed. Cir. 1987); In re Fine, 5 USPQ 2d 1596 (Fed. Cir. 1988). The mere fact that references can be combined does not render the resulting combination obvious unless the prior art also suggests the desirability of a combination and merely indicating that isolated elements recited in the claims are known is not a sufficient basis for concluding that the combination of claimed elements would have been obvious. ACS Hospital Systems, Inc. v Montefiore Hospital, 221 USPQ 929 (Fed. Cir. 1984); Ex Parte Hiyamizu, 10 USPQ 2d 1393 (Bd. Pat. App. & Int. 1988). Furthermore, it is well established that the references must suggest what applicants have done when viewed alone, and not in retrospect or with the use of a hindsight analysis. In re Shaffer, 108 USPQ 326 (CCPA 1956).

When the law is applied to the claimed invention and the art cited by the Examiner, the sole conclusion that can be drawn is that the claims are not rendered obvious because there is no teaching, suggestion or incentive supporting the combination of the cited references. In fact, it is only through the use of a hindsight analysis using the Applicants' teachings in the application that the Examiner is able to establish an argument for obviousness. As is well developed in the caselaw pertaining to 35 USC 103, the use of hindsight in an analysis of obviousness is improper. The Examiner has combined the disparate teachings of the cited references to reach a conclusion of obviousness absent any teaching, suggestion or incentive that would have led one of ordinary skill in the art to combine the relevant teachings of the references. At best, the claimed invention may be "obvious to try" but this is not the standard upon which obviousness is determined. In re O'Farrell, 7 USPQ 2d 1673 (Fed. Cir. 1988). None of the references suggest the combination of performing multiple rounds of transformation in a plant plastid utilizing the same selectable marker gene in a manner allowing for the excision of the marker gene using a recombinase system. Nor is there any suggestion whatsoever that this combination would have any reasonable expectation of success. Applicants' successful efforts to combine the usefulness of plastid transformation with a recombination system to provide an elegant and unique method for performing multiple rounds of plastid transformations while utilizing the same selectable marker gene should be rewarded. This rejection should be withdrawn.

**Conclusion**

Applicant respectfully requests reconsideration on the merits of the application as a whole. The Examiner is encouraged to call the undersigned should any further action be required for allowance.

Respectfully submitted,



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